I, 30.8. Found: C, 37.8, 37.9; H, 3.6, 3.8; S, 7.71, 7.75; I, 31.1, 31.3.

While an almost complete replacement by iodide could be achieved by longer heating, no well-defined product was isolated.

Anhydridization of 1,4-Sorbitan (Arlitan).—Ten grams of 1,4-sorbitan was mixed with 0.5 g. of concentrated sulfuric acid and heated at 140° in an oil-bath for one hour. The liquid was then heated to 165–170° and evacuated to about 5 mm. pressure whereupon a nearly colorless liquid distilled. On seeding the distillate with isosorbide, immediate crystallization occurred. The crude product weighed 7.1 g. (79%); melted at 58–59° (cor.). After one recrystallization, it melted from 60–61° (cor.).

The preparation was successfully repeated with a sample of 0.5 g. of 1,4-sorbitan and one drop of sulfuric acid.

Anhydridization of 3,6-Sorbitan.—A sample of 0.83 g. of 3,6-anhydrosorbitol[14] was treated with two drops of concentrated sulfuric acid and heated in an oil-bath at 120–140° for three quarters of an hour. A light yellow liquid was formed. On reducing the pressure to 3 mm. and gradually raising the bath temperature to 160° a colorless liquid distilled. On being seeded with isosorbide, the distillate crystallized to a solid mass. The weight was 0.49 g. (67%) and the crude product melted from 59–60° (cor.).

Non-formation of Isosorbide by Anhydridization of 1,5-Sorbitan (Polygalitol).—A sample of 0.1469 g. of polygalitol was treated with one drop of concentrated sulfuric acid and heated in a bath at 145° for an hour in a small molecular still constructed from two test-tubes. The still was then evacuated to 2-mm. pressure and slowly warmed. A minute quantity of colorless sirup collected on the condenser. Dissolved in pyridine and treated with an excess (0.376 g.) of benzoyl chloride, this material gave a water-insoluble sirup which did not crystallize.

Pure sorbitol treated by the same micro technique readily yielded dibenzoylisosorbide identical with that described.

Summary

The crystalline dianhydrosorbitol discovered by Harden has been prepared by improved methods and its physical constants measured. The substance has been shown to contain the 1,4 and 3,6 anhydro rings and free secondary hydroxyl groups. The dibenzoate and di-*p*-toluenesulfonate have been described as well as a product formed from the latter by replacement of one tosylate group by iodide. It has been shown that isosorbide is formed by further anhydridization of either 1,4-sorbitan or 3,6-sorbitan but not from 1,5-sorbitan. The observation that 1,6-dibenzoylsorbitol is dehydrated directly to dibenzoylisosorbide in boiling acetylene tetrachloride indicates that benzoyl groups shift position under these conditions and invalidates the conclusions of Brigl concerning the structure of several mannitol anhydrides.

CAMBRIDGE, MASS.
WILMINGTON, DEL. RECEIVED JANUARY 29, 1946

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, AND FROM THE RESEARCH DEPARTMENT, ATLAS POWDER COMPANY]

Hexitol Anhydrides.[1] The Structures of the Anhydromannitols of Brigl and Grüner.[2] The Structure of Isomannide

BY R. C. HOCKETT,[3] H. G. FLETCHER, JR.,[3] ELIZABETH L. SHEFFIELD,[3] R. MAX GOEPP, JR.,[3] AND SOL SOLTZBERG[3]

Brigl and Grüner[4] have reported that when 1,6-dibenzoylmannitol is heated in boiling acetylene tetrachloride with a little *p*-toluenesulfonic acid as a catalyst, three transformation products are formed. To these compounds they assigned the following structures: A = 2,4-monoanhydromannitol 1,6-dibenzoate; B = 2,4,3,5-dianhydromannitol 1,6-dibenzoate; C = 2,5-monoanhydromannitol 1,6-dibenzoate.

In making these structure assignments, Brigl and Grüner assumed first of all that the benzoyl groups remain in their original positions during reaction. Since, however, we have recently shown that the benzoyl groups of the analogous 1,6-dibenzoylsorbitol shift their positions under the same conditions[1] it has seemed necessary to review the conclusions of these German workers with respect to the mannitol anhydrides.

A repetition of the experimental procedure described by these authors has yielded us three products whose physical constants agree with those reported. We have concluded, however, that the structures of the first two are actually these: A = 1,4-monoanhydromannitol 2,6 (or 3,6) dibenzoate; B = 1,4,3,6-dianhydromannitol 2,5-dibenzoate.

The third product (C) is discussed more fully in a later paper of this series.

The experimental observations and the chain of reasoning which led us to these structure assignments will be given in some detail since they represent general procedures capable of wide application.

---

[1] The previous paper of this series, THIS JOURNAL, **68**, 927 (1946).

[2] Parts of the material in this paper are taken from theses submitted to the Graduate School of the Massachusetts Institute of Technology in partial fulfillment of the requirements for the degree of Doctor of Philosophy by H. G. Fletcher, Jr., in September, 1942, and by Elizabeth L. Sheffield in October, 1944. A part of the material was contained in a paper read before the Division of Sugar Chemistry and Technology at the Detroit meeting of the American Chemical Society in April, 1943.

[3] Present addresses: R. C. Hockett, Sugar Research Foundation, 52 Wall Street, New York, N. Y.; H. G. Fletcher, Jr., National Institute of Health, Bethesda, Maryland; Elizabeth L. Sheffield, Massachusetts Institute of Technology, Cambridge, Mass.; R. Max Goepp, Jr., and Sol Soltzberg, Atlas Powder Co., Wilmington, Del.

[4] (a) Brigl and Grüner, *Ber.*, **66B**, 1945–1949 (1933); (b) **67B**, 1582–1589 (1934); *cf.* Hockett and Fletcher, THIS JOURNAL, **66**, 469 (1944).

By means of methanolic ammonia[5] we removed the benzoyl groups of the substance A and obtained a crystalline monoanhydromannitol (mannitan) melting at 146–147°. The behavior of this compound toward lead tetraacetate identifies it quite clearly as the 1,4-anhydromannitol.[6]

According to theory, nine mannitans are possible. These are listed with their predicted behavior toward lead tetraacetate.

TABLE I

MANNITANS

No.	Structure	Moles of $Pb(OAc)_4$ consumed	Moles of HCHO formed	Type of oxidation curve[a]
1	1,2 (or 5,6)	3	1	Erythritol VI_3
2	1,3 (or 4,6)	2	1	Glycerol VI_2
3	1,4 (or 3,6)	1	0	Mannofuranoside V
4	1,5 (or 2,6)	2	0	Gulopyranoside I
5	1,6	3	0	?
6	2,3 (or 4,5)	2	1	Glycerol VI_3
7	2,4 (or 3,5)	1	1	Ethylene glycol VI_1
8	2,5	1	0	*Trans*-cyclohexandiol
9	3,4	2	2	Erythritol VI_3

[a] Reference 6.

The accompanying graph (Fig. 1) shows that only one molar equivalent of lead tetraacetate is consumed before a sharp break occurs in the curve. This oxidation curve is analogous to that of methyl mannofuranoside, and formaldehyde is produced only in a trace.

Furthermore, 1,4-mannitan is a known substance. It was prepared by Valentin in 1936[7] by an application of the method of Fischer and Zach[8] which should yield a product of unquestionable authenticity without any possibility of a Walden inversion. The physical constants of Valentin's mannitan agree well with those recorded by Brigl and Grüner and by ourselves, a fact which Valentin did not observe.

TABLE II

Author	M. p., °C.	Rotation, deg.[a]
Brigl and Grüner	146	−24.2 (*c*, 1.159, H_2O)
Valentin	145–148	−23.75
Hockett, *et al.*	146.2–146.8 (cor.)	−23.7 (*c*, 1.043, H_2O)

[a] Reference 14.

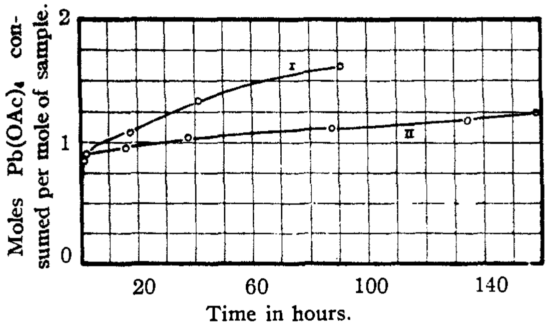
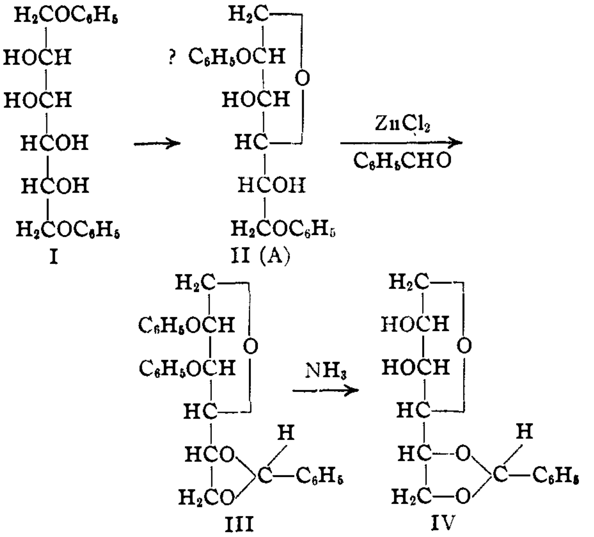


Fig. 1.—The oxidation of 1,4-anhydromannitol (I) and 5,6-benzolidene-1,4-anhydromannitol (II) by lead tetraacetate.

We have also confirmed the observation of Brigl and Grüner that when substance A (II) is treated with zinc chloride and benzaldehyde, a monobenzylidenedibenzoylmannitan (III) is formed. The removal of benzoyl groups with methanolic ammonia[5] produced a new substance, a monobenzylidenemannitan (IV). The oxidation of this product by lead tetraacetate showed it to be the 5,6-monobenzylidene-1,4-anhydromannitol. No formaldehyde was produced but one mole of lead tetraacetate was consumed at a rate closely similar to that shown by 1,4-mannitan itself (Fig. 1). The monobenzylidenedibenzoylmannitan must therefore be esterified in the two and three positions as shown in formula III.



In substance A itself, however, the benzoyls cannot be in these positions or the compound would be attacked by lead tetraacetate which is not the case. The conclusion is forced upon us that at least one benzoyl shifts during acetalation (II → III). This explains why Brigl and Grüner were unable to obtain an isopropylidene derivative of A under mild conditions. In A, therefore, one benzoyl must be either in the 2 or 3 position and the other in the 5 or 6 position. The more probable assumption is that the latter still occupies its original 6 position. The choice of structures is therefore narrowed to two possibilities as indicated in the introduction.

By treating our monobenzylidene-1,4-mannitan (IV) with zinc chloride and benzaldehyde, we obtained a 2,3,5,6-dibenzylidene-1,4-mannitan (V) which melts at 122–123°. For this derivative, Valentin[7] reports 125–126°.

---

[5] The method was described by Brigl and Grüner, *Ber.*, **67**, 1585 (1934), but was not applied by them directly to the substance A.

[6] *Cf.* Hockett, Conley, Yusem and Mason, THIS JOURNAL, **68**, 922 (1946), for the analogous case of arlitan.

[7] Valentin, *Coll. Czechoslov. Chem. Comm.*, **8**, 35 (1936).

[8] Fischer and Zach, *Ber.*, **45**, 2070 (1912). *Cf.* Hockett, Nickerson and Reeder, THIS JOURNAL, **66**, 472 (1944).

TABLE III

ISOMANNIDE

Source	1,6-Dibenzoylmannitol	Mannitol and H_3PO_4 or H_2SO_4	Mannitol and formic acid		Heating of 1,6-dichloro-1,6-didesoxymannitol
M. p., °C.	86.5–87.0	86.0–86.5	87	87	87
$[\alpha]_D$ in H_2O[a]	+90.7 (*c*, 2.9)	+90.9 (*c*, 2.96)	+91.36 (*c*, 6)	..	..
Author	Hockett *et al.*	Hockett *et al.*	Fauconnier	Krantz *et al.*	Wiggins[b]

[a] Reference 4. [b] Reference 12.

As a result of these various considerations, we may conclude that the structure of Brigl and Grüner's "2,4-monoanhydromannitol" is established definitely as 1,4-monoanhydromannitol.[9]

We proceed now to consideration of compound B which is a dibenzoyldianhydromannitol (IV). Brigl and Grüner removed the benzoyl groups from this substance with methanolic ammonia and obtained a sirupy mannide which they considered to be a new isomer of the known mannides.[10] On repeating this debenzoylation, however, we obtained a crystalline product which is evidently identical with Fauconnier's crystalline "isomannide"[11] (VII). We have also prepared isomannide repeatedly from mannitol by the direct action of heat and sulfuric or phosphoric acid. Such samples of isomannide, when benzoylated, produce a dibenzoylisomannide identical with B (IX).

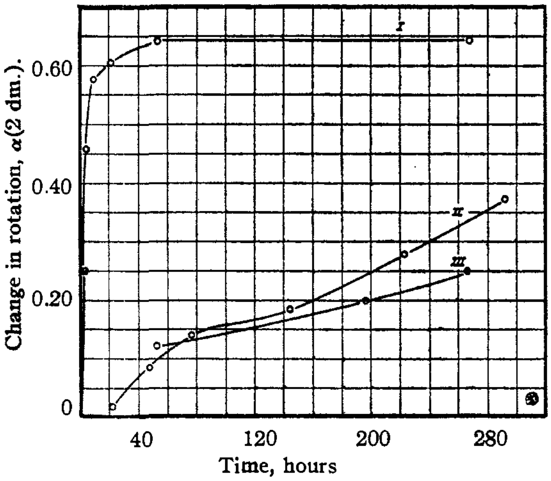


Fig. 2.—Reactions of anhydropolyols with triphenylchloromethane in pyridine solution: I, 1,4-anhydromannitol; II, isosorbide; III, isomannide.

The question of the structure of substance B therefore resolves itself into the problem of determining the structure of isomannide.[12] Brigl and Grüner[4] showed that the dibenzoate of their monoanhydromannitol (which we now regard as the 1,4) is converted on further heating in acetylene tetrachloride into the dibenzoate of the dianhydride which we now know to be isomannide. Finally, by the action of barium hydroxide, Brigl and Grüner obtained a partial cleavage of their dianhydride (isomannide) back into 1,4-mannitan. These observations prove that isomannide contains the 1,4-ring.

Mathematically, twenty-seven dianhydromannitol structures are possible. Of these only six contain the 1,4 or 3,6 ring and are therefore to be considered as possibilities.

TABLE IV

MANNIDES WITH 1,4(3,6) RING

	Structure	No. of primary OH groups	Moles of $Pb(OAc)_4$ consumed	Moles of HCHO formed
1	1,2,3,6(1,4,5,6)	0	1	0
2	1,4,2,3(3,6,4,5)	1	1	1
3	1,4,2,5(2,5,3,6)	1	0	0
4	1,4,2,6(1,5,3,6)	0	0	0
5	1,4,3,5(2,4,3,6)	1	0	0
6	1,4,3,6	0	0	0

The observation that isomannide is unattacked by lead tetraacetate eliminates the 1,4,2,3(3,6,4,5) and 1,2,3,6(1,4,5,6) structures as possibilities.

The question whether isomannide contains any primary hydroxyl group becomes crucial in choosing among the remaining four structures. Brigl and Grüner[4] concluded that both hydroxyl groups are primary because di-*p*-toluenesulfonylisomannide (VIII) underwent the iodide replacement reaction when heated with sodium iodide in acetone solution for three and a half hours at 110°. We have repeated this reaction under similar conditions and obtained an identical product. Nevertheless, as indicated in the previous paper of this series,[1] we do not consider the reaction to be diagnostic of the presence of primary groups.

As a further means of investigating the ques-

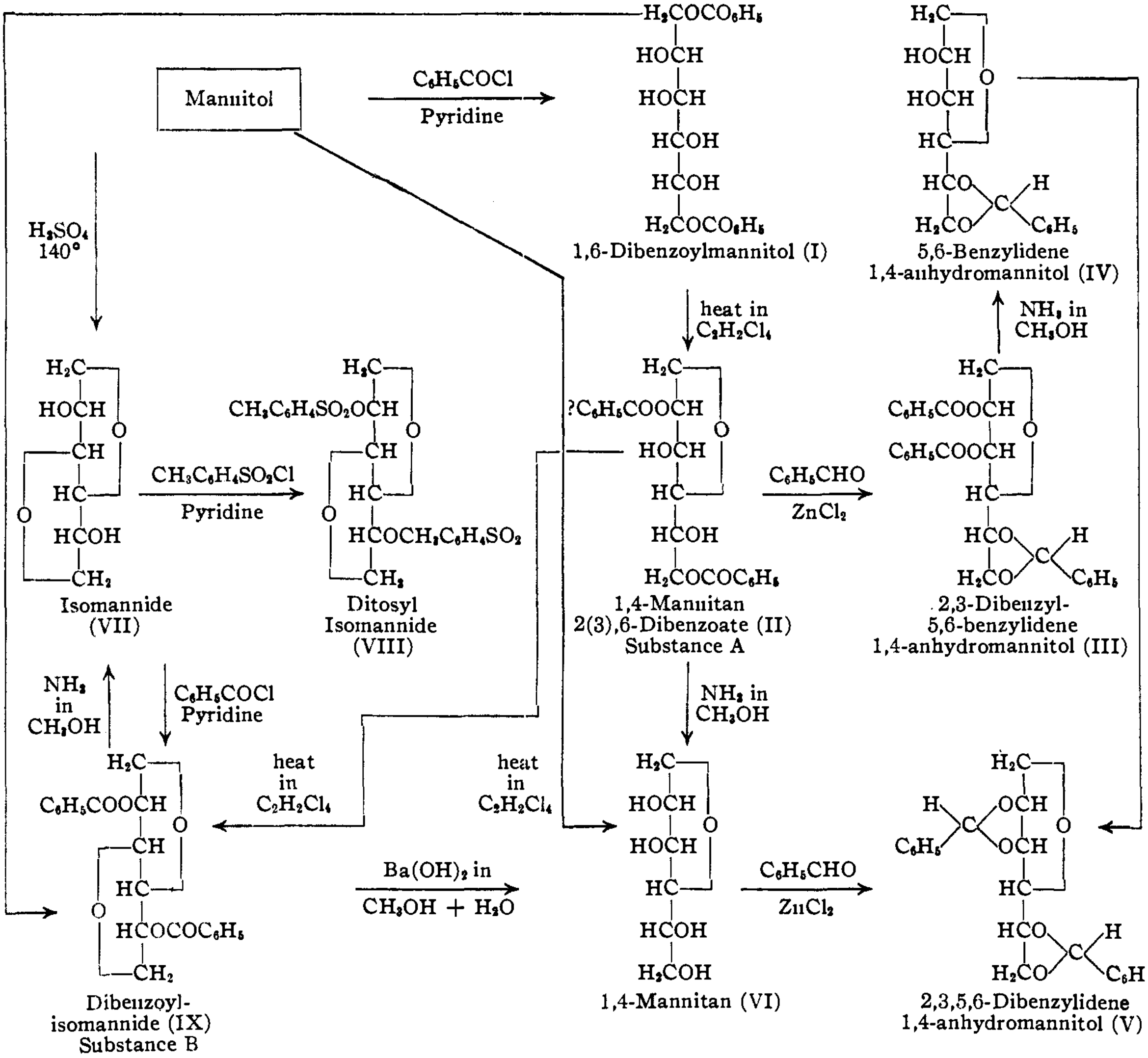
---

(9) It is highly probable that the crystalline α-mannitan of Bouchardat, *Ann. chim.*, (5) **6**, 103 (1875), is also 1,4-mannitan since it is reported to rotate −23.8° (*c*, 7, H_2O, 14°) although the recorded melting point of 137° is low. Van Romburgh and van der Burg [*Proc. Roy. Acad. Amsterdam*, **25**, 339 (1922)] also have reported a sirupy mannitan to which they assign the 1,4 ring. This product was identified only as the crystalline diacetonate melting at 155°. A diacetonate has not been prepared for comparison from authentic 1,4-mannitan.

(10) (a) "Mannide," Berthelot, *Ann. chim.*, (3) **47**, 312 (1856); (b) "Isomannide," Fauconnier, *Bull. soc. chim.*, (2) **41**, 119 (1884); (c) Alekhine, *ibid.*, **42**, 328 (1885); (d) "β-Mannide," Siwolobow, *Ann.*, **233**, 368 (1886).

(11) *Cf.* also Krantz, Oakley and Carr, *J. Phys. Chem.*, **40**, 151 (1936).

(12) A solution of this question has recently been published by Wiggins, *J. Chem. Soc.*, 4 (1945); *cf.* Fletcher and Goepp, THIS JOURNAL, **67**, 1042 (1945). However, since we reached the same conclusions independently by methods of wide applicability, a complete account of our work will be given. Conclusions concerning the structure of isomannide were announced by Hockett, Sheffield and Goepp before the Division of Sugar Chemistry and Technology, at the New York meeting of the American Chemical Society in September, 1944.



tion, we measured the relative rates of the tritylation of 1,4-mannitan and isomannide (Fig. 2). The former compound reacted so much faster that we consider the evidence to be strongly against the presence of a primary group in isomannide.

If no primary hydroxyl group is present in isomannide, structures 3 and 5 are eliminated from consideration, leaving only the 1,4,2,6(1,5,3,6) and the 1,4,3,6 structures as possibilities. The synthesis of authentic 1,5,3,6-dianhydromannitol is described in the next paper.

Experimental

1,6-Dibenzoylmannitol (I).—The compound was prepared as described by Brigl and Grüner[13] except that separation from tribenzoylmannitol was effected by trituration of the crude product with acetone, the less soluble dibenzoate being left as a residue. This product was then anhydridized without further purification.

Anhydridization of 1,6-Dibenzoylmannitol.—Several preparations were made exactly as described by Brigl and Grüner.[4] In addition, an experiment was performed in which 300 g. of crude 1,6-dibenzoylmannitol (0.77 mole) and 0.75 g. of *p*-toluenesulfonic acid were added to three liters of commercial xylene and the mixture boiled under reflux for three hours. Solution was complete in one hour; after three hours, 20 cc. of water had been collected in a graduated Barrett receiver, corresponding to an elimination of 1.47 moles of water per mole of dibenzoylmannitol.

The acid was neutralized with sodium bicarbonate and the xylene was removed under diminished pressure. Trituration of the residue with acetone eliminated insoluble unchanged dibenzoylmannitol. The acetone extract was then evaporated dry and the residue crystallized fractionally from denatured alcohol. Two fractions corresponded to compounds A and B of Brigl and Grüner: (A) 15 g. of material melting at 142–145° (Brigl and Grüner give 142° for "2,4-anhydromannitol dibenzoate"); (B) 33 g. of material melting at 131–132° (Brigl and Grüner give 131–132° for their dianhydromannitol dibenzoate).

Isomannide (VII) from Brigl and Grüner's "Dianhydromannitol Dibenzoate."[4]—A sample of the dibenzoyldianhydromannitol (compound B) was subjected to debenzoylation with methanolic ammonia as described by Brigl and Grüner.[5] Instead of the sirupy product described by these authors, we obtained a crystalline product, which was purified by recrystallization from alcohol. After purification,

---

[13] Brigl and Grüner, *Ber.*, **65B**, 642 (1932); *cf.* Hockett and Fletcher, THIS JOURNAL, **66**, 469 (1944).

it melted at 86.5–87° and rotated[14] +90.7° (*c* 2.9, H_2O, 23°). Rebenzoylation with benzoyl chloride in pyridine gave a dibenzoyldianhydromannitol melting at 131–132°. When mixed with an authentic sample of dibenzoylisomannide (see below), the melting point was not depressed.

1,4-Mannitan (VI) from Fraction A.—The debenzoylation of this material was carried out with methanolic ammonia according to the procedure described by Brigl and Grüner[5] for debenzoylation of another substance but not applied by them in the case of this particular dibenzoylmonoanhydromannitol. We obtained crystals which after purification by recrystallization from alcohol, melted at 146–147°, and rotated[14] −23.7° (*c* 1.043, H_2O). Brigl and Grüner obtained the same monoanhydromannitol by simultaneous debenzoylation and opening of one ring of dibenzoyldianhydromannitol with barium hydroxide. Their product also melted at 146°.

Rate of Oxidation of 1,4-Mannitan by Lead Tetraacetate (see Fig. 1).—A sample of 0.0410 g. or 0.00025 mole of substance was oxidized by lead tetraacetate at a molar ratio of 8.64 moles of the oxidant to substrate in a 100.0-cc. volume of acetic acid at 20°. These are not quite the standard conditions later established by Hockett, Dienes and Ramsden[15] but in analogous cases no significant differences in the type of oxidation curve have been observed under these two slightly different sets of conditions.

2,3-Dibenzoyl-5,6-benzylidene-1,4-mannitan (III).—This substance, described by Brigl and Grüner[4b] as "1,6-dibenzoyl-2,4-anhydro-3,5-benzal-mannit" was prepared as described by these authors through the action of benzaldehyde and zinc chloride on Fraction A (or dibenzoyl-1,4-mannitan). Our product, crystallized from alcohol, melted at 161–162°. Brigl and Grüner give 162°.

5,6-Benzylidene-1,4-mannitan (IV).—By debenzoylating 2,3-dibenzoyl-5,6-dibenzylidene-1,4-mannitan with methanolic ammonia as described by Brigl and Grüner[5] for another substance, we obtained a substance melting at 143–144°.

Anal. Calcd. for $C_{13}H_{16}O_5$: C, 61.9; H, 6.35. Found: C, 61.6, 61.8; H, 6.30, 6.25.

This product was not made by Brigl and Grüner.

Rate of Oxidation of 5,6-Benzylidene-1,4-mannitan by Lead Tetraacetate (see Fig. 2).—This oxidation was carried out under exactly the standard conditions described by Hockett, Dienes and Ramsden.[15]

2,3,5,6-Dibenzylidene-1,4-mannitan (V).—This substance was obtained by treating 5,6-benzylidene-1,4-mannitan with benzaldehyde and zinc chloride according to the procedure described by Brigl and Grüner[4b] but not applied by them to the present case. It melted at 122–123°. When prepared directly from 1,4-mannitan the product had the same melting point and a mixture of the two samples melted without depression. Valentin[7] reports a melting point of 125–126° for the substance.

Preparation of Isomannide from Mannitol.—In a typical preparation, ten grams of pure mannitol was placed in a 50-cc. distilling flask with a wide side arm (10 mm.) located low on the neck of the flask. Twenty-five drops (0.820 g.) of concentrated sulfuric acid was added from a capillary pipet and the mixture then heated in an oil-bath. A brief heating at 170° melted the mannitol and the mixture was homogenized by gentle shaking. It was then kept at 140° for one hour. A tared receiver was attached and the apparatus evacuated to 2-mm. pressure. Heat was applied by an oil-bath and at 130° a clear, viscous liquid distilled which promptly crystallized in the receiver. The process was halted when foaming of the residue threatened to contaminate the distillate. The yield was 2.76 g. or 34% of the theoretical and the somewhat hygroscopic product melted at 83.6° (cor.). When purified by recrystallization from ethyl acetate, it melted at 86.0–86.5° and rotated[14] +90.85 (*c* 2.54, H_2O, 28.6°).

Dibenzoylisomannide (IX) from Isomannide.—The 2.76 g. of isomannide prepared as described, was dissolved in 30 cc. of pyridine and the cooled solution was treated with 5 cc. (6.07 g.) of benzoyl chloride added dropwise. The mixture was kept at 60° for fifteen minutes and then poured in a fine stream into 200 cc. of water with stirring. During refrigeration overnight, the precipitated oil became crystalline. Collected on a filter and recrystallized from 30 cc. of alcohol, the crop of large needles weighed 4.4 g. or 65.7% of the theoretical. The product melted at 142.1–142.4° (cor.) and was soluble in acetone and hot alcohol but sparingly soluble in cold alcohol and insoluble in water.

Ditosylisomannide (VIII).—A sample of 10.2 g. of isomannide (0.07 mole) was dissolved in 60 cc. of pyridine and mixed with a solution of 28 g. (0.148 mole) of *p*-toluenesulfonyl chloride in 75 cc. of pyridine. The mixture stood at room temperature for six hours and was then warmed on a steam-bath for one hour. It was then cooled and poured over 500 g. of crushed ice.

The separated ester became crystalline at once and, after the ice melted, was collected on a filter, washed with several liters of water and dried. The crude product was recrystallized from 250 cc. of methanol with a yield of 19 g. or 59% of the theoretical. It melted at 88.5–90.2°. Brigl and Grüner[4b] report a melting point of 89–90°.

Diiodidesoxyisomannide.—Ditosylisomannide (3 g., 0.0066 mole), sodium iodide (2.5 g., 0.0166 mole), and 30 cc. of acetone were heated in a sealed tube at 120° for three hours. At the end of this period, the tube was opened, and the sodium *p*-toluenesulfonate was collected on a filter and washed with 40 cc. of acetone. The acetone solution with the washings was evaporated dry under diminished pressure. The residue was dissolved in 100 cc. of ether and washed with three 33-cc. portions of 2% sodium thiosulfate solution to remove iodine. After drying over anhydrous sodium sulfate, the ether was evaporated under diminished pressure. The residue crystallized when rubbed with 10 cc. of methanol at 0°. After three recrystallizations from 6 cc. of methanol, a yield of 1.4 g. of product melting at 61–62° was obtained, or 58% of the theoretical. Brigl and Grüner report a melting point of 69–70°.

Rate of Tritylation of Isomannide (Fig. 2).—A sample of 1.13 g. of isomannide (0.00768 mole) was dissolved in 50 cc. of pyridine. A solution of 8.6168 g. of freshly prepared triphenylchloromethane in 50 cc. of pyridine was made and, at a noted time, the two solutions were mixed. Readings of the rotation of the mixture were made at intervals while the temperature was kept at 23–25°.

Ditritylisomannide (Dr. Morris Zief).—The solution remaining from the rate-of-tritylation measurement was left at room temperature for about two and a half years. Water was then added dropwise and the triphenylcarbinol which separated was collected on a filter. Further addition of water gave a precipitate which was colorless after two recrystallizations from aqueous alcohol. This substance softened at 85° and melted at 92–94°. The rotation[14] in chloroform was +44.3° (*c* 0.38, 27°).

Anal. Calcd. for $C_{44}H_{38}O_4$: C, 83.81; H, 6.03. Found: C, 83.8, 83.9; H, 6.17, 6.20.

This is a new substance.

Summary

The anhydridization of 1,6-dibenzoylmannitol by heating in high-boiling solvents as first described by Brigl and Grüner has been repeated. The benzoylated mono- and dianhydromannitols described by the German authors have been obtained but the structures assigned by these authors have not been confirmed. The monoanhydromannitol described by Brigl and Grüner as "2,4-anhydromannitol" has been shown by us to be identical with the 1,4-anhydromannitol described by Valentin. The latter structure has also

---

[14] All rotations cited in this paper are specific rotations of the D line of sodium at 20° unless otherwise specified. Concentrations are grams of substance in one hundred cubic centimeters of solution.

[15] Hockett, Dienes and Ramsden, THIS JOURNAL, **65**, 1474 (1943).

been confirmed by the behavior of the substance toward lead tetraacetate. The dianhydromannitol described by Brigl and Grüner as "2,4,3,5-dianhydromannitol" has been shown by us to be identical with isomannide, and the structure of the latter has been shown to be either 1,5,3,6- or 1,4,3,6-dianhydromannitol. Several derivatives of these anhydrides described by Brigl and Grüner have been reprepared and their structural assignments corrected. Two new compounds have been prepared: 5,6-benzylidene-1,4-anhydromannitol and ditritylisomannide.

CAMBRIDGE, MASS.
WILMINGTON, DEL. RECEIVED JANUARY 29, 1946

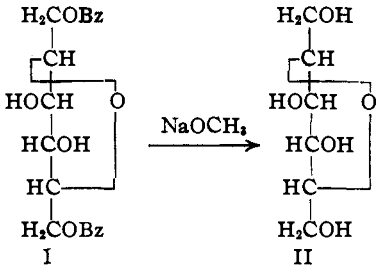
[CONTRIBUTION FROM THE SUGAR RESEARCH FOUNDATION LABORATORY, DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, AND THE RESEARCH DEPARTMENT, ATLAS POWDER COMPANY]

Hexitol Anhydrides.[1] The Structure of the "2,5-Anhydromannitol" of Brigl and Grüner[2] (2,5-Anhydrosorbitol)

BY R. C. HOCKETT,[3] MORRIS ZIEF[3] AND R. MAX GOEPP, JR.[3]

In an earlier paper of this series,[4] we described a repetition of the anhydridization of 1,6-dibenzoylmannitol according to the procedure of Brigl and Grüner[5] and indicated that we succeeded in obtaining the same three products described by the German workers. However, the structures assigned to two of these products were altered as a result of our investigations.[1,4]

The third product described by Brigl and Grüner was considered by them to be 2,5-monoanhydro-1,6-dibenzoylmannitol (I). A substance of this structure should be oxidized by lead tetraacetate according to theory, since it contains an unsubstituted pair of hydroxyl groups in a vicinal relation. Nevertheless the German authors described the compound as inactive toward lead tetraacetate. Because of its behavior when oxidized by permanganate, they nevertheless considered the structure assignment to be appropriate and ascribed the inactivity toward lead tetraacetate to the fact that the free hydroxyl groups bear a *trans* relation to each other in space.



I II

However, when we subjected our sample of the same compound to lead tetraacetate oxidation under the standard conditions used in this Laboratory for rate-of-oxidation measurements,[6] we found that oxidation does occur (Fig. 1). One molar equivalent of oxidant is consumed at a low rate of speed, exactly according to the prediction of theory. The very much more rapid oxidation of 1,4-anhydromannitol or of methyl α-D-mannofuranoside is plotted for comparison.

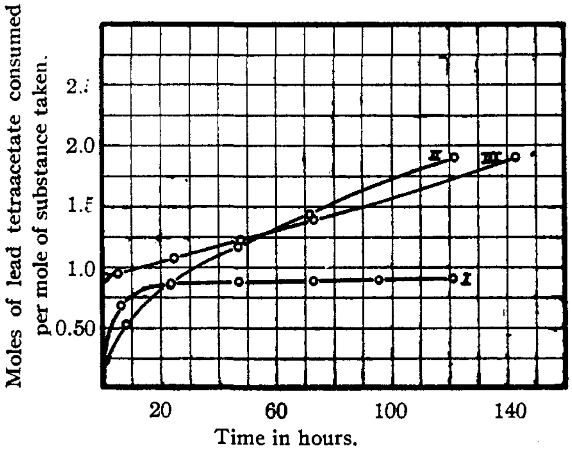


Fig. 1.—Oxidation of 2,5-monoanhydro-1,6-dibenzoylmannitol and 2,5-monoanhydromannitol: I, 2,5-monoanhydro-1,6-dibenzoylmannitol (2,5-monoanhydro-1,6-dibenzoylsorbitol); II, 2,5-monoanhydromannitol (2,5-monoanhydrosorbitol); III, methyl α-D-mannofuranoside.

The benzoyl groups of the compound were removed by sodium methylate to produce a sirupy mannitan (II). On oxidation under standard conditions, a less useful curve was obtained since the reaction rate did not diminish sharply after consumption of one molar equivalent of oxidant (Fig. 1). It was ascertained, however, that no significant quantity of formaldehyde is produced by the oxidation of the debenzoylated substance. Reference to the table indicating predicted be-

---

[1] The previous paper of this series, THIS JOURNAL, 68, 930 (1946).

[2] Most of the material in this paper was presented before the Division of Sugar Chemistry and Technology of the American Chemical Society at the Cleveland Meeting in April, 1944.

[3] Present addresses: R. C. Hockett, Sugar Research Foundation, 52 Wall Street, New York, N. Y.; Morris Zief, Department of Chemistry, Massachusetts Institute of Technology, Cambridge 39, Massachusetts; R. Max Goepp, Jr., Atlas Powder Company, Wilmington, Delaware.

[4] Hockett, Fletcher, Sheffield, Goepp and Soltzberg, THIS JOURNAL, 68, 930 (1946).

[5] Brigl and Grüner, *Ber.*, 66, 1945 (1933); 67, 1582 (1934).

[6] Hockett, Dienes and Ramsden, THIS JOURNAL, 65, 1474 (1943).